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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,220	12/04/2006	Craig B. Thompson	130694.01201	4279
34136	7590	12/02/2010	EXAMINER	
Pepper Hamilton LLP 400 Berwyn Park 899 Cassatt Road Berwyn, PA 19312-1183			LOVE, TREVOR M	
			ART UNIT	PAPER NUMBER
			1611	
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			12/02/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/556,220	Applicant(s) THOMPSON ET AL.	
	Examiner TREVOR M. LOVE	Art Unit 1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 September 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 8-10, 12-21, 23-26, 36, 49-52 and 58-74 is/are pending in the application.
- 4a) Of the above claim(s) 9 and 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8, 10, 12-20, 23-26, 36, 49-52 and 58-74 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>08/24/2010 09/27/2010</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Acknowledgement is made to Applicant's response filed 09/27/2010.

Claims 1-6, 8-10, 12-21, 23-26, 36, 49-52, and 58-74 are pending.

Claims 9 and 21 are withdrawn.

Claims 1, 4, 5, 6, 10, 16, and 52 are currently amended.

Claims 68-74 are newly added.

Claims 1-6, 8, 10, 12-20, 23-26, 36, 49-52, and 58-74 are currently under consideration.

Note: Applicant's election of record includes:

Invention I (claims 1-26, 35-37, and 49-53)

Glioblastoma cells as the cancer cell species

Hydroxycitrate as the ATP citrate lyase inhibitor species

Phosphoenolpyruvate as the tricarboxylate inhibitor species

Withdrawn Rejections and/or Objections

The objection to claims 4-6 because of the following informalities: the claims recite "...effective amount of a an ATP..." is withdrawn in view of Applicant's amendments to said claims.

The rejection of claim 7 under 35 U.S.C. 103(a) as being unpatentable over Kuhajda et al. (US Patent 5,759,837, Patent issued Jun. 2, 1998), in view of Schroder et al. (1999, Int. J. Gynecol Cancer) is withdrawn in view of Applicant's cancellation of said claim.

The rejection of claim 7 under 103(a) as being unpatentable Kuhajda et al. (US Patent 5,759,837, Patent issued Jun. 2, 1998), in view of Schroder et al. (1999, Int. J. Gynecol Cancer) as applied to claims 1-8, 10, 12-15, 50-52, and 58-65, and further in view of Bru et al. (US Patent 5,219,846, Patent issued Jun. 15, 1993) is withdrawn in view of Applicant's cancellation of said claim.

Maintained Rejections

-note: New Grounds necessitated by amendment for newly added claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

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were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, 10, 12-15, 50-52, 58-65, 68-72, and 74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuhajda et al. (US Patent 5,759,837, Patent issued Jun. 2, 1998), in view of Schroder et al. (1999, Int. J. Gynecol Cancer).

Kuhajda teaches methods of treating carcinomas comprising administering a compound that inhibits fatty acid synthase (FAS), including inhibitors of citrate lyase such as hydroxycitrate (see Abstract, column 3, line 52-54 and column 11, lines 22-34 and 60). Kuhajda teaches that since many tumor cells are extremely dependent on endogenous fatty acid synthesis, lower FAS activity levels need not exclude a specific tumor as a candidate for therapy with fatty acid synthase inhibitors (see column 7, lines 61-64). Kuhajda teaches that it is advantageous to combine the active of Kuhajda with chemotherapeutic agents to target rapidly cycling cells (see column 8, lines 53-65). Kuhajda teaches that the presence of FAS in cells of the carcinoma may be detected by any suitable method, including activity assays, stains, and immunoassays (see column 7, line 65 to column 8, line 22).

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Kuhajda fails to directly teach that the cancer is identified as comprising cancer cells that have a high rate of aerobic glycolysis, that said cancer is identified by PET imaging utilizing ^{18}F -fluoro-deoxyglucose (^{18}F -FDG), or that said cancer is glioma.

Schroder teaches the role of ^{18}F -fluoro-deoxyglucose positron emission tomography (^{18}F -FDG PET) in diagnosis of cancer. Schroder states that the clinical significance and usefulness of PET has been proven for a variety of malignant tumors, and specifically names glioma (see page 117, columns 1 and 2). Schroder teaches that “[i]n 1931 Warburg demonstrated that malignant tumors are characterized by an elevated aerobic and anaerobic glycolysis” (see page 117, first sentence).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the ^{18}F -FDG PET imaging as taught by Schroder to diagnose a patient with cancer for treatment with the composition of Kuhajda. One would have been motivated to do so since Schroder teaches that ^{18}F -FDG PET imaging is useful in diagnosing malignant cancers, which, according to Warburg as cited by Schroder, necessarily comprises elevated aerobic glycolysis. There would be a reasonable expectation of success in utilizing the diagnostic method of Schroder to diagnose a carcinoma which is to be treated with the composition of Kuhajda since Kuhajda teaches that the carcinoma may be detected by any suitable method (see Kuhajda, column 7, line 65 to column 8, line 22).

It would further have been obvious to one of ordinary skill in the art at the time the invention was made to treat a cancer patient with a FAS inhibitor and a different chemotherapeutic agent or radiation therapy to control tumor growth. One would have

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been motivated to do so because Kudhajada suggest that FAS inhibitors may be utilized in conjunction with other therapeutic programs, wherein Kudhajada states that chemotherapy and radiation therapy are the most common forms of tumor treatment (see column 1, lines 36-43 and column 8, lines 58-65).

Response to Arguments

Applicant argues in the remarks filed 09/27/2010 that Kuhajda discloses methods of treating individuals who have cancer that is dependent on endogenously synthesized fatty acid, which is contrary and teaches away from the teachings of claims 10, 12-15, and 65. Applicant's argument is not found persuasive since as can be seen by column 7, lines 61-64 of Kuhajda, "lower FAS activity levels need not exclude a specific tumor as a candidate for therapy with fatty acid synthase inhibitors". Therefore, one of ordinary skill in the art would recognize the usefulness of the treatment of Kuhajda on the instant tumors as well as those which are dependent on endogenously synthesized fatty acids. Applicant further argues that PET FDG technology has limitations which makes the use thereof "limited since PET FDG requires enhanced uptake of labeled glucose" (see remarks, page 13). Applicant's argument is not found persuasive since Schroder clearly teaches "the clinical significance and usefulness of PET has been proven for a variety of malignant tumors, i.e., pancreatic carcinoma, glioma, etc.," (see Schroder, page 117, paragraph bridging columns 1 and 2, emphasis added). It is noted that Applicant's evidence provided has been considered, but has not overcome the clear teaching in Schroder. Applicant further argues that the patient population is not identical, and the pathway to be inhibited is different, one skilled in the art could not use

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the teachings of the two references to produce the claimed invention. Applicant's argument is not found persuasive since Schroder teaches that identifying glioma with PET FDG is well known and useful, and Kuhajda teaches treatment of tumors with the instant actives wherein said tumors can be identified by any known means. Therefore, one of ordinary skill in the art would readily arrive at the instant method given the teachings of Kuhajda and Schroder.

Claims 1-6, 8, 10, 12-20, 36, 49-52, 58-74 are rejected under 103(a) as being unpatentable Kuhajda et al. (US Patent 5,759,837, Patent issued Jun. 2, 1998), in view of Schroder et al. (1999, Int. J. Gynecol Cancer) as applied to claims 1-6, 8, 10, 12-15, 50-52, 58-65, 68-72, and 74, and further in view of Bru et al. (US Patent 5,219,846, Patent issued Jun. 15, 1993).

The teachings of Kuhajda and Schroder are set forth above under the discussion of claims 1-6, 8, 10, 12-15, 50-52, 58-65, 68-72, and 74.

Kuhajda and Schroder fail to directly teach that the composition further comprises a tricarboxylate transporter inhibitor, namely phosphoenolpyruvate (elected species).

Bru teaches methods for treating human tumors, particularly tumors that have become resistant to chemotherapy comprising administering an effective amount of phosphoenolpyruvic acid (see Abstract and column 1, lines 41-64).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the phosphoenolpyruvic acid of Bru with the citrate lyase

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inhibitor (e.g. hydroxycitrate) of Kuhajda for additive anti-tumor effects. One would have been motivated to do so since Kuhajda teaches that FAS inhibitors (e.g. ATP lyase inhibitors) can be combined with other chemotherapeutic agents and phosphoenolpyruvic acid as taught by Bru is a chemotherapeutic agent. It is further noted that MPEP 2144.05 states: “It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art.” *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); and *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992).

Response to Arguments

Applicant argues in the remarks filed 09/27/2010 that the teachings of Bru do not cure the deficiencies identified above for Kuhajda and Schroder. Applicant's arguments are not found persuasive since the alleged deficiencies are not found persuasive as identified above. Applicant further argues that Schorder "while teaching the use of PET to identify ovarian tumors, does not disclose glioma as set forth in claim 66". Applicant's argument is not found persuasive since Schroder clearly teaches "the clinical significance and usefulness of PET has been proven for a variety of malignant tumors, i.e., pancreatic carcinoma, glioma, etc.," (see Schroder, page 117, paragraph bridging columns 1 and 2, emphasis added). It is noted that Applicant's evidence provided has been considered, but has not overcome the clear teaching in Schroder.

Conclusion

No claims allowed. All claims rejected. No claims objected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **TREVOR M. LOVE** whose telephone number is (571)270-5259. The examiner can normally be reached on Monday-Thursday 7:30-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TL

/David J Blanchard/
Primary Examiner, Art Unit 1643